PROFILE OF ABNORMAL RESULTS OF CONVENTIONAL COAGULATION TESTS IN TRAUMA PATIENTS

DISSERTATION

SUBMITTED FOR

M.D.IN PATHOLOGY

THE TAMILNADU DR.M.G.R MEDICAL UNIVERSITY

DEPARTMENT OF PATHOLOGY

PSG INSTITUTE OF MEDICAL SCIENCE & RESEARCH

PEELAMEDU, COIMBATORE- 641 004

TAMILNADU, INDIA

CERTIFICATE

This is to certify that the dissertation work entitled **"Profile of Abnormal Results of Conventional Coagulation Tests in Trauma Patients"** submitted by Dr.S.Aravinth is work done by him during the period of study in this department from 30/05/2009 to 29/05/2012. This work was done under the guidance of **Dr.T.M.SubbaRao,** Professor, Department of Pathology, PSG IMS&R.

Dr. Alamelu Jayaraman
Professor & HOD, Pathology
PSGIMS & R
Coimbatore – 04

Dr.S.Ramalingam
Principal
PSGIMS & R
Coimbatore – 04

CERTIFICATE

This is to certify that the thesis entitled **"Profile of Abnormal Results of Conventional Coagulation Tests in Trauma Patients"** submitted by Dr.S.Aravinth to the Tamilnadu Dr MGR Medical University, Chennai, for the award of the degree of **Doctor of Medicine in Pathology,** is a bonafide record of research work carried out by him under my supervision. The contents of this thesis, in full or in parts, have not been submitted to any other Institute or University for the award of any degree or diploma.

Coimbatore
21.11.2011

Dr T M SubbaRao
Professor of Pathology
PSG IMS&R
Coimbatore - 641004

ACKNOWLEDGEMENT

First of all, I express my sincere gratitude to my guide, Dr. T. M. SubbaRao, Professor of Pathology, for having conceptualized and designed the thesis proposal. His guidance helped in the metamorphosis of the raw data collected by me, to a scientific treatise.

I am grateful to Dr. Ramalingam (Principal), Dr. Vimal Kumar (Medical Director) and Dr. Alamelu Jayaram (HOD, Pathology) for the necessary permissions granted and for the excellent amenities offered to carry out my study. I wish to thank Dr. Ramalingam in particular, for having critiqued my thesis proposal prior to its execution.

My thanks to Professors Dr.V.Nirmala and Dr.S.Shanthakumari and also to the Associate Professors, Dr.Suma B Pillai and Dr.V.Sandhya, for having permitted me to visit the Clinical Pathology laboratory whenever I had a case pertaining to my study.

The Assistant Professors Dr.Chetana Sharma, Dr.Uma Maheswari, Dr.S. Vidyalakshmi, Dr.M.N.Savithri, Dr.M.Kanmani Devi, Dr.P.Pavithra and Dr.V.Chaitra provided the much needed moral support. I thank all of them for that.

My thanks to my fellow postgraduates Dr.Volga, Dr.Yegumuthu and Dr.Usha for their constant aide memoire to complete the project on time!

I express my appreciation to my junior postgraduate colleagues for having helped me in the data collection activity and sharing my regular work when I was held up with work relating to my study.

I am indebted to all the patients of my study for their kind participation and to the faculty and staff of EMD department and to all the technical staff of Clinical Pathology Laboratory for having spared their time and effort towards my thesis work.

I acknowledge the Clinical Biochemistry laboratory team for their role in analysis of samples.

Last but not the least, I express thanks to my wife Dr. Senthur Selvi for her patience and for verifying typographical and syntax errors.

CONTENTS

INTRODUCTION:

Trauma is a serious global health problem accounting for approximately 1 in 10 deaths worldwide[1]. Approximately 50% of trauma related deaths occur immediately and these deaths can only be avoided by injury prevention. 30% of the trauma patients die during the initial hours post injury and preventing these deaths is the goal of modern trauma care. The commonest cause for this death is uncontrolled non-surgical hemorrhage. This is potentially preventable. Hence identification of the cause of bleeding and effective control of bleeding is expected to decrease mortality. All of this has to be achieved in the 'Golden Hour' i.e. within 1 hour of a severe injury.

Life threatening bleeding in trauma patients due to vascular injury often requires surgical intervention. Sometimes arterial embolization may be required in patients with multiple trauma. A review of recent literature shows an acute 'Coagulopathy of Trauma' (COT) as a distinct entity and is said to be present in 1 of 4 severely injured trauma patients in the western world when tested within 1 hour of admission. This caused diffuse bleeding [exsanguination] and is more difficult to manage and requires transfusion by fresh frozen plasma, platelets and coagulation factor

concentrates instead of the conventional intravenous fluids, plasma expanders and packed cells alone. The diagnosis of this acute coagulopathy can be made by performing basic tests for coagulation such as Prothrombin time (PT), partial thromboplastin time (APTT) and D-dimer.

We did a thorough search of literature in subscribed journals of our institute (print & online), pubmed, Ovid, Google, etc., to look for the prevalence of Coagulopathy of Trauma in trauma patients. Almost all the publications are from the western world (Europe and North America). There are isolated publications from India on the prevalence of Coagulopathy of Trauma in Orthopedic trauma and head injury.

All trauma patients undergo basic investigations such as complete blood counts, urinalysis, X-rays, etc. However PT, APTT and D-dimer tests are not performed routinely in most trauma centers including the Emergency Medicine Department of PSGIMSR Hospitals.

This study was basically carried out to identify the occurrence of Coagulopathy of Trauma in severely injured patients brought to Emergency Medicine Department of PSGIMSR Hospitals, using basic screening tests for coagulation such as Platelet count, PT, APTT & D – dimer and also to observe if there was any correlation between the

abnormal results of coagulation and the injury in terms of site and severity. If the occurrence was high, it would justify the need to perform these screening tests in all patients with severe injury, as a routine, so that, with appropriate patient care, it could translate to better outcomes in terms of morbidity and mortality.

AIMS & OBJECTIVES:

1. To observe the incidence of abnormal results of basic tests for coagulation in severely injured trauma patients received at PSGIMS&R Hospital.

2. To observe if there is a correlation between abnormal results of coagulation and injury by site.

REVIEW OF LITERATURE

India has seen a sea change in urbanization and industrialization in the past two decades. With mechanization and revolution in technology coupled with increased motorization injuries have become a major public health problem in India[2].

Injuries account for 2% of all of the causes of death in children under 5 years while cutting across all ages, injuries rank nineth in the list of all cause mortality in India[3]. According to the mortality fact sheet released by the World Health Organization in 2006, out of every 1000 deaths, 189 are due to road traffic accidents[3].

Tamilnadu ranks second in the list of Indian states that have witnessed the accelerated motorization of their cities and villages[2]. 71% of these vehicles are composed of two wheelers that account for 60% of the Road Traffic Accidents[2].

Angela Sauaia, Frederick Moore et al published their audit findings on causes of all the trauma deaths that occurred in the Denver city and county during 1992. They observed that exsanguinations accounted for 39% of the deaths that occurred within 24 hours in trauma patients[4].

The first major article which identified the presence of life threatening coagulopathy in trauma patients was published by the same team in 1997 in the Journal of Trauma. They prospectively analyzed data of patients who were more than 15 years old and had received multiple transfusions. They found that those who required multiple product transfusions had elevated levels of Prothrombin time (PT) and Activated Partial Thromboplastin Time (APTT)[5]. Based on their observations of the case records they concluded that persistent hypothermia and progressive metabolic acidosis were predictors of post injury life-threatening coagulopathy.

Jana Macleod, Mauricio et al published their study on the **incidence of coagulation abnormalities in early trauma**, in the Journal of Trauma in 2003. They reviewed prospectively collected data on trauma patients presenting to University of Miami / Jackson Memorial hospital, Miami, Florida between the period 01/01/1995 and 31/12/2000. This hospital is a Level I Trauma centre. They performed a logistic regression analysis on the results of PT, APTT and platelet count and concluded that when an initial abnormal PT was observed in trauma patients, it increased the

adjusted odds of dying by 35%, while an initial abnormal APTT increased the adjusted odds of dying by 326%[6]!

In the same year, Karim Brohi et al published a path breaking article on Acute Traumatic Coagulopathy in the Journal of Trauma[7]. They commented that **Coagulopathy of Trauma (COT)** is usually attributed to dilution of coagulation factors from intravenous fluid therapy or massive blood transfusion. However there have been only few studies that examined the state of the hemostatic system immediately after injury, before resuscitation began. Their study addressed this by a large retrospective analysis of data from different trauma registers. They concluded that COT was present even before treatment / resuscitation began and that it was not related to fluid administration.

Karim Brohi et al opined that **COT was probably mediated by the release of chemical mediators** that activated the multiple humoral systems including coagulation, fibrinolysis, complement and Kallikrein cascades. They also observed that there was a higher incidence of COT in brain injury patients, which could be due to the release of brain tissue thromboplastin after neuronal injury.

The September 2004 issue of the American Journal of Surgery featured another article by Jana Macleod along with 3 other co-authors[8]. They published their results of analysis of data of a large cohort of population from the Trauma Registry of the Emny University Hospital, Atlanta, Georgia. The prime purpose of their analysis was to identify risk factors for death from trauma. Based on their observations, they concluded that **prognostic indicators for all-cause mortality after trauma** which remained independent in the presence of all other factors and are potentially treatable included elevated PT, elevated APTT, low hemoglobin, low systolic blood pressure and elevated base deficit. The untreatable, independent indicators of mortality included head injury, increasing age and a high injury severity score.

Spahn and Rossaint published a review article on the pathophysiology of Coagulopathy of Trauma in the British Journal of Anesthesiology, in 2005[9]. This document till date remains the most widely accepted **review on the pathophysiology of COT**. The following text describes the pathophysiology proposed by the authors in their own words. “Hemostatic responses to vascular injury consist of a series of interactions between the subendothelial matrix, platelets and coagulation proteins resulting in a

stable fibrin clot. In addition, thrombin activates the thrombin-activable-fibrinolysis inhibitor which protects the clot from premature fibrinolysis. The pathophysiology of COT is complex. The precise cause is difficult to identify and is likely to be multifactorial. They are blood loss, consumption of platelets and coagulation factors, dilution of coagulation factors and platelets, increased fibrinolysis, impaired function of platelets and coagulation factors, coagulation- compromising effects of colloids, hypothermia, hypocalcemia etc". The authors quoted the study of Simmons and colleagues who had showed that there was an increase in fibrinolytic activity immediately following trauma. This fibrinolytic activity returned to normal after the first 24 hours in patients with mild to moderate injury, but remained elevated in those with major injuries. The fibrinolytic activity was more conspicuous in trauma patients who were hypothermic.

The interrelation between hypothermia, metabolic acidosis and progressive coagulopathy has been referred to as the 'lethal triad'. Each factor exacerbates the others, leading to life-threatening bleeding or exsanguinations.

The causes of hypothermia are multifactorial and interdependent. These include decreased heat production due to tissue hypoperfusion in hemorrhagic shock, altered central thermoregulation and infusion of inadequately warmed resuscitation fluids and blood components[10]. The deleterious effects of hypothermia on the coagulation process are due to the fact that the coagulation process is temperature dependent and function optimally at 37^0C.

Spahn and Rossaint expressed their disappointment that the commonly used tests for the measurement of haemostatic competence, such as PT and APTT have never been validated for their predictive value in trauma or surgery settings[9]. They suggested that repeated measurements of fibrinogen levels and thromboelastograph (for analysis of platelet function) could be helpful in providing ideal component therapy in Trauma patients.

The hypothesis that **COT was more common in brain injuries** was tested by Pathak et al in the Department of Neurosurgery at Post-graduate Institute of Medical Education and Research, Chandigarh[11]. They collected samples from different areas of brain from ten cadavers (which served as

controls) and from contused brain tissue obtained after surgery in patients with head injury(test samples). They observed that the Tissue Thromboplastin (TTP) activity of the frontal, parietal and temporal lobes after head injury was significantly raised in contrast to the control group, thus highlighting the role of TTP in coagulopathy following head injury.

Marc Maegel et al published the results of their large retrospective analysis of the German Trauma Registry database which included 17,200 multiple injured patients[12]. They observed that 34.2% of all injured patients showed evidence of coagulopathy upon admission to the emergency room as evidenced by elevated PT and low platelet count (<1,00,000/mm^3). Post treatment coagulopathy was observed in 40% of the remainder and these were common in those patients who received > 4000ml of IV fluids in 24 hours. In patients who received < 500ml of IV fluids in 24 hours, the incidence of post admission coagulopathy was only 10%. Overall 28% of injury patients who had COT upon admission in the emergency room died.

Karim Brohi, Mitchell Cohen and Ross Davenport performed a meta-analysis of all the data in the literature (including their own publications) on the incidence, risk factors, pathogenesis, clinical trials and management guidelines for Acute Coagulopathy of Trauma. They published their

observations as a review article, in the 'Current Opinion in Critical Care' journal in 2007[13]. They observed that COT was unassociated with dilution, hypothermia, acidemia associated platelet dysfunction or consumption of coagulation proteases. They opined that shock is the prime initiator of COT. **They postulated that the systemic anticoagulation of COT was due to activation of the Protein C pathway**. In the absence of hypoperfusion, trauma activated the extrinsic pathway ultimately generating thrombin which cleaved fibrinogen from fibrin. In the presence of tissue hypoperfusion, the endothelium expressed thrombomodulin which complexes with thrombin to divert it to an anticoagulant function. Less thrombin was available to cleave fibrinogen and thrombin complexed to thrombomodulin activated Protein C, which inhibited the extrinsic pathway through cofactors V and VIII. The authors admit that this hypothesis which was based on results of other studies needed to be corroborated with an assay of activated Protein C levels. The authors also observed that there was evidence of increased fibrinolytic activity in trauma patients. The authors observed that all the retrospective studies which identified the presence of COT, all had used variants of PT and APTT for diagnosis.

Although more patients had an abnormal PT than APTT, it was APTT which appeared more specific in predicting the outcome. The authors also remark that there has been no assessment of clot quality or strength, fibrinolytic activity or platelet function.

Raised D-dimer levels following injury have been identified in many studies. Activation of fibrinolysis occurred as tissue plasminogen activator (tPA) was released from the endothelium following injury and ischemia. Satoshi Gando, Ichiro Tedo & Munehiro Kubota determined the effects of Disseminated Intravascular Coagulation (DIC) and head injury on post trauma coagulation and fibrinolysis. They measured 6 types of coagulation and fibrinolytic molecular markers including D-dimer assay immediately after trauma, 3 days later and 6 days later. They observed that when trauma was complicated with DIC, the molecular markers showed significantly higher values than those for non-DIC patients on all days. In the head-injured patients, such effect was not noted.

There is **only one study of platelet function in trauma patients** by Jacoby RC, Owing JT, Holmes et al[14]. Overall, they observed an increase in platelet function, but non-survivors showed a decrease in platelet function compared with controls. Karim Brohi et al have reviewed this

article also and observed that it was difficult to interpret these results in the light of our current knowledge of early coagulopathy and it remained to be determined if platelet function tests are useful for diagnosis or guiding therapy in trauma patients.

Karim Brohi and John Hess with ten other co-authors once again published **another review article on the mechanisms of COT in 2008** in the Journal of Trauma Injury, Infection and Critical care[15]. The authors formed a group called The 'Educational Initiative on Critical Bleeding in Trauma' (EICBT) which was an independent, international medical collaboration that aimed to increase awareness among health care professionals that COT may play a crucial role in patients' outcomes. They performed a comprehensive search of literature using the indexed online database MEDLINE / Pubmed. Boolean operators and MeSH- thesaurus keywords were applied as a standardized use of language to unify differences in terminology into single concepts. They reviewed a total of 87 full publications which included those that met full selection criteria as well as additional relevant publications. They observed that **there are 6 key initiators of COT** viz., tissue trauma, shock, hemodilution, hypothermia,

acidemia and inflammation. Injury severity was closely associated with the degree of coagulopathy. However if tissue injury was unassociated with physiologic derangement, coagulopathy was rare. Hyperfibrinolysis was common after trauma and was a direct consequence of both tissue injury and shock, mediated principally by the release of tissue plasminogen activator from the injured endothelium. The authors noted that tissue trauma was an initiator of coagulation and fibrinolysis, but in isolation rarely caused clinical coagulopathy. Hence they recommended that the term 'DIC' to describe COT was misleading both in terms of the process involved and as a paradigm to direct subsequent therapy. The authors noted that shock itself appeared to be a prime driver of early coagulopathy and that there was a dose-dependent association between the severity of tissue hypoperfusion and the degree of admission coagulopathy as measured by PT and APTT. **In combination, direct tissue trauma and shock with systemic hypoperfusion appeared to be the primary factors responsible for the development of COT.**

Hemodilution, hypothermia and acidosis which were ruled out as causes for COT in earlier reviews have found their place back in the pathogenesis of COT in this review by Karim Brohi, John Hess et al! The dilution of

coagulation factors caused by shift of fluid from interstitial spaces to plasma and the attendant dilution of coagulation factors by resuscitation using intravenous fluids accounted for clinical coagulopathy in trauma. The authors suggest that blood component therapy must be administered in the ratio of 1:1:1 of red cell: plasma: platelets to avoid the effect of dilution on clinical coagulopathy. Many studies had showed that clinically significant effects on plasma coagulation, platelet function and clinical bleeding were seen in moderate hypothermia at temperature below 34^0C, thus accounting for the **role of hypothermia in COT**. Acidemia (caused by low fluid shock states and excess ionic chloride administered during resuscitation) itself impaired the function of plasma proteases. Inflammation has been also found to be a co-driver for COT, as there was a significant cross talk between coagulopathy and inflammation systems.

David Hoyt, Richard Dutton, Carl Hauser et al conducted a qualitative International survey of clinical practice among senior physicians responsible for the treatment of patients with multiple injuries i.e. with Injury Severity Score (ISS) that was $\geq$16. They observed that there were regional differences in trauma management decisions. **PT, APTT, ISS, Platelet counts and temperature were the most common criteria used**

to assess COT in most centers[16]. Only 19% of the centers also evaluated the fibrinolytic pathway. Hence they recommended the need for common definition of coagulopathy and standardized clinical protocols to ensure optimal patient care.

Peep Talving, Rodd Benfield, Pantelis Hadjizacharia et al in their prospective study of traumatic brain injury associated COT found that COT occurred in 36% of all patients and in 34% of patients with isolated head injury[17]. They also observed that **COT was especially higher in severe penetrating head injuries**.

John Hess, Allison Lindel, Lynn G. Stansbury et al conducted a retrospective observational study to describe a relationship of injury to COT. They observed that brain injury was associated with a distinct coagulopathy. **They concluded that basic coagulation tests such as PT, APTT, platelet count and fibrinogen concentration appeared to be sensitive tools for identifying patients with COT who were at a high risk of early death[18].**

Ganter MT and Pittet JF published a review article on new insight into acute coagulopathy in trauma patients in 2010[19]. They observed that COT

was found in 25% of trauma patients with major injuries and that these patients had a worse clinical outcome. Tissue trauma, systemic hypoperfusion and hyperfibrinolysis caused by overt activation of Protein-C pathway were responsible for the development of COT.

The lone study on COT from India was published in the Journal of Emergencies, Trauma and Shock in the year 2010[20]. This prospective study was performed in **All India Institute of Medical Sciences**, New Delhi where they followed up 48 patients admitted with orthopedic trauma. They checked laboratory parameters such as PT, APTT, TT, fibrinogen assay, D-dimer and platelet counts on all these patients. These tests were performed first at the time of admission, second at the time of surgery and third at the post operative period. Healthy hospital and laboratory staffs served as controls. They observed that mild derangement of coagulation profile was found in 18% of patients on admission. This increased to 26% on the day of surgery. While fibrinogen levels showed a progressive increase since the time of admission to the post operative period, D-dimer levels showed no significant pattern. Most of the platelet count variations were at the time of injury. Per-operative and post-operative changes in platelet counts were very minimal.

MATERIALS AND METHODS

This study was a **prospective observational study**. The study period was from 20th January 2011 to 30th June 2011. The study population was from all the patients who attended the Emergency Medicine Department [EMD] of PSGIMSR Hospital, Coimbatore. We included all the trauma patients and excluded those patients presenting with medical and non-traumatic surgical emergencies to the EMD. Further, trauma patients who had reported after an initial treatment from another hospital or from a clinic were also excluded.

The paramedical team of the Emergency department evaluated the trauma patient at the site of trauma or immediately on arrival and derived a primary triage scale which guided the team in prioritizing evacuation and care. The triage scale was a 5 level scale [1 to 5] ranging from those who needed immediate intervention to those in whom medical intervention could be delayed upto 2 hours.

The primary triage scale followed by the paramedical team in the EMD department of PSGIMSR hospital is an adaptation of the FRENCH scale, version 2[21], which is furnished in Table 1.

Table 1: FRENCH scale: General description of triage and the actions considered

Triage	Description	Action
1	Immediately life-threatening	Action focused on support of one or more vital functions Immediate medical and paramedical intervention
2	Marked impairment of a vital organ or imminently life-threatening or functionally disabling traumatic lesion	Actions focused on treatment of the vital function or traumatic lesion Immediate paramedical and medical intervention within 20min
3	Functional impairment or organic lesions likely to deteriorate within 24hr or complex medical situation justifying the use of several hospital resources	Multiple actions focused on diagnostic evaluation and prognostic evaluation in addition to treatment Medical intervention within 60min +/- followed by paramedical intervention
4	Stable, noncomplex functional impairment or organic lesions, but justifying the urgent use of at least one hospital resource	Consultation with limited diagnostic and/or therapeutic procedures Medical intervention within 120min +/- followed by paramedical intervention
5	No functional impairment or organic lesion justifying the use of hospital resources	Consultation with no diagnostic or therapeutic procedure Medical intervention within 20 min

Patients were attended to, based on the primary triage scale. The entire clinical information was entered in a standard assessment form which had details on the triage scale, arrival mode, mechanism of injury, date, time

and site of injury etc. A secondary triage was performed subsequently by medical personnel (Trauma care physicians, orthopedic surgeons and anesthesiologists), skilled nurses and paramedics on the status of airway and circulation (based on blood pressure and pulse rate value), reaction of pupils etc. Based on this clinical assessment (called primary survey) of eye opening, a verbal and motor response, the Glasgow Coma Scale Score was obtained. Based on the systolic blood pressure, respiratory rate and Glasgow coma scale, a Revised Trauma Score [RTS] over a total score of 12 was obtained. Table 2 shows the parameters and scores used to obtain the Revised Trauma Score.

The Revised Trauma Score [RTS] which was derived by the trauma care physician provided a comprehensive assessment of the patient's status as it was more objective. It assessed the severity of injury more precisely and guided management protocols. Based on the scores, trauma patients were finally classified into 4 groups as shown in Table 3.

Table 2- Revised Trauma Score

Systolic BP	>89 mm Hg	4
	76-89 mm Hg	3
	50-75 mm Hg	2
	1-49 mm Hg	1
	Nil	0
Respiratory Rate	10-29/min	4
	>29	3
	6-9	2
	1-5	1
	0	0
GCS	13-15	4
	9-12	3
	6-8	2
	4-5	1
	3	0
Total		----/12

Table 3 – Grouping of patients according to the severity of injury

RTS score	Patient labeled as	Management plans
12 / 12	Delayed (walking wounded)	These patients were treated only after the Urgent & Immediate groups were treated.
11/12	Urgent	Intervention is required but the patient can wait for a short time. These were treated after the immediate group patients.
4/12 to 10/12	Immediate	Immediate intervention was necessary.
≤3/12	Morgue	Unlikely to survive. As resources are scarce, trauma team focuses on patients of above groups as they are more likely to survive.

The study population was those patients who had a RTS between 4 & 11 as these were considered to have severe injuries that required Urgent / Immediate intervention.

A secondary survey was performed subsequently on all trauma patients, where **details of injuries sustained was noted**. This included site of injury, description of the wounds, neurovascular deficits etc.

All the patients were subjected to relevant radiological investigations such as Chest X rays, CT scan, MRI scan, Ultrasound etc.

All of the patients were also subjected to standard laboratory tests such as Complete Blood counts, Blood Group, Plasma glucose and serum electrolytes, as part of the existing protocol at the EMD.

Samples for Complete Blood Counts and Blood Group were sent in **lavender topped vacutainers** with K_3EDTA as the anticoagulant.

Our study was to observe if there were abnormalities in Prothrombin Time [PT], Activated Partial Thromboplastin Time [APTT] and D-dimer, in those who were severely injured [ie RTS between 4/12 & 11/12].

The blood samples for PT and APTT testing were collected in blue topped vacutainers which had 0.3ml of 3.2% sodium citrate in it. 2.7 ml of blood was added, to maintain the blood: anticoagulant ratio as 9:1. **For D-dimer analysis 2ml of blood was collected in green topped vacutainers** which had heparin as the anticoagulant. The principal investigator conducted two sessions on the methodology of sample collection to the nursing staff of the EMD. Further, they were informed that the blood drawal should only be performed after an informed consent was obtained from the patient. If the patient was not in a state to give consent [as assessed by the resuscitation team], it was required to be obtained from the nearest relatives who had accompanied the patient. If relatives were not present on admission the nursing team ought to contact them by telephone (if the number was known) and obtain an initial oral consent, and the relative could sign subsequently on arrival to the hospital. The costs for the tests were borne by the institute as part of a post-graduate thesis grant. Patients for whom consent was not obtainable or declined to consent were also excluded from the study.

The **hemoglobin and platelet counts** were tested in the Clinical Pathology lab using the **Beckman Coulter cell counter of model LH 750** [Figure 1]. This machine utilizes the principle of **Volume-Conductivity-Scatter (VCS) Technology.** The volume is measured physically by impedance technology. The conductivity of cells is assessed by radiofrequency range altering current. The scatter of the laser beam which is struck on the cells is detected by a median angle light scatter signal. By this technology three independent energy sources are used to probe approximately 8192 cells in their near native state.

Figure 1: The Beckman Coulter LH 750 cell counter used for estimation of Hemoglobin & Platelet counts

For the estimation of hemoglobin, a lytic agent was used which converted the hemoglobin to a stable pigment. The absorbance of the pigment was directly proportional to the hemoglobin concentration of the sample. The transmittance of light of 525nm wavelength through a standard path length of hemoglobin solution was compared to the transmittance of such light in the same way through a reagent blank. The platelet count was principally done by volume analysis by impedance method. During sensing, pulses that represents cells from 2-20fl are classified as platelets. The system also plotted platelet histograms using platelet pulses.

The **Prothrombin time and Activated Partial Thromboplastin time** were estimated using a fully automated, bench top, hemostasis analyzer called **Stago - STA compact** (Figure 2). This is a continuous random access instrument that performs clotting assay by **electromechanical principle** as well as chromogenic and immunological assays. PT and APTT performed on this machine are not affected by lipemic or icteric samples because the determinants did not depend on light absorbance. Even though this machine could estimate D-dimers using the immunological assay it was not performed as the procedure was not standardized in the lab.

.

Figure 2: The Stago STA compact machine used to estimate PT & APTT

D-dimer was estimated using COBAS Integra-400. It works with the principle of particle enhanced **immunoturbidimetric assay**. Latex particles of uniform size are coated with monoclonal antibodies to the D-dimer epitope. The antigen or antibody complex produced by the addition of samples containing D-dimer leads to an increase in the turbidity of the test reactants. The precipitate was determined turbidimetrically at 659nm.

Results of all the relevant blood tests were entered in the master chart where the relevant clinical data was already entered. Using a Microsoft

excel spread sheet, the occurrence of COT and the relationship between severity of injuries and abnormal results of coagulation were analyzed.

OBSERVATION AND RESULTS

The study period was from 20th January 2011 to 30th June 2011. During this period, 8019 patients reported to the Emergency Medicine Department of PSGIMSR Hospitals. Of these, 1310 patients were trauma patients and of the remainder 5029 were admitted for medical emergencies and 1680 for non-traumatic surgical emergencies [Table 4]. Thus 16.4% of patients who reported to the EMD were trauma patients.

Of the 1310 trauma patients admitted during the study period, 312 were referred from other smaller hospitals (in and around Coimbatore) or had received initial treatment in a doctor's clinic and referred subsequently to PSGIMSR Hospital for further care. Hence they were excluded. Thus, the number of trauma patients who were admitted to PSGIMSR Hospital directly was 998.

Table 4: Details of patients admitted to EMD during the study period and a general analysis of type of emergency

Type of Emergency	Sub classification of causes of emergency	No of patients	Grant total
Medical emergencies	Chest pain	475	**5029**
	Stroke	186	
	Poisoning	264	
	Fever	3800	
	Referral for thrombocytopenia management	50	
	Others	254	
Non-traumatic surgical emergencies	Acute abdomen	1214	**1680**
	Diabetic foot dressing	56	
	Non traumatic bleeds eg: epistaxis, ear bleeds	31	
	Others	379	
Traumatic injuries			**1310**
Grant total			**8019**

Of the 998 patients, 43 were brought dead. Thus the number of trauma patients alive on admission was 955. These patients were subcategorized based on the Revised Trauma Score as shown in Table 5.

Table 5: Sub-categorization of trauma patients based on RTS.

RTS score	No of patients	Remarks
12 / 12 [Delayed]	655	Excluded from study
11/12 [Urgent]	153	**Study population [269]**
4/12 to 10/12 [Immediate]	116	
≤3/12 [Morgue]	31	Excluded from study
Total	955	

Most of the trauma patients [69%] had minor injuries where the treatment could be delayed up to 2 hours, while, 3.25% had very severe injuries that were unlikely to survive. Hence both of these groups were excluded. The remainder 269 patients who had severe injuries as identified by RTS scores between 11/12 and 4/12 were included.

Of the 269 patients who were eligible for the study, the trauma team could obtain consent from 62 patients only which formed the final study group on whom the PT, APTT and D-dimer tests were performed.

Figure 3 shows the algorithm which depicts the manner in which the final study population was arrived at.

Of the 62 patients of the study population, 54 were male [87%] and 8 were female. Table 6 shows the sex-wise distribution of patients according to the severity of injury.

Figure 3: Algorithm depicting derivation of study population

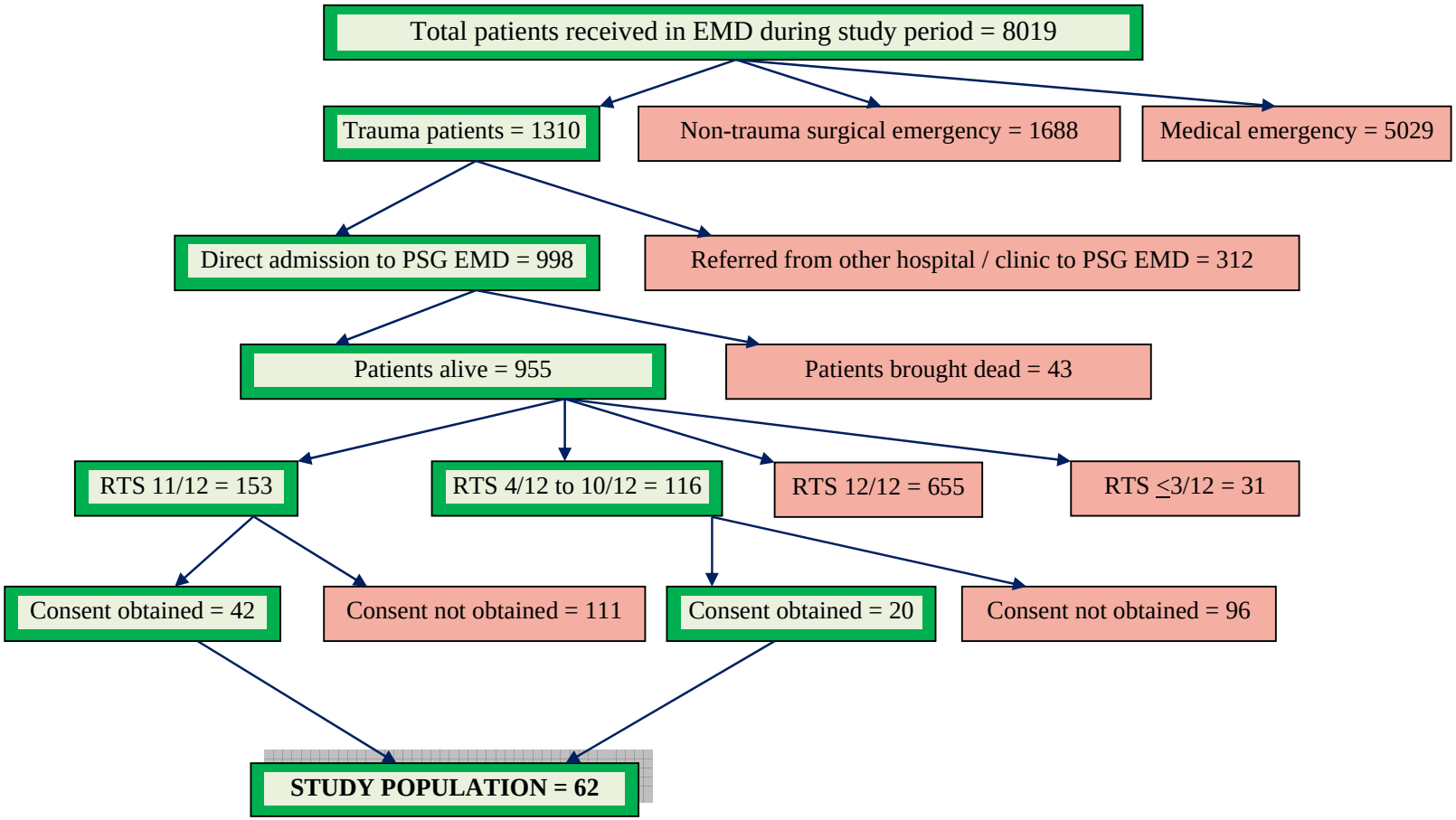


Table 6: Sex distribution of the study population according to the severity of injury

RTS	No of male	No of female	Total
11/12	35	7	42
4/12 to 10/12	19	1	20
Total	54	8	62

Most of the patients were aged between 21 and 40 (51.6%). The youngest patient was 7 years old and the oldest was 81 years old. A second peak in the 6th decade was noted [21%]. Figure 4 shows the age distribution of the study population.

Figure 4: Age distribution of the study population

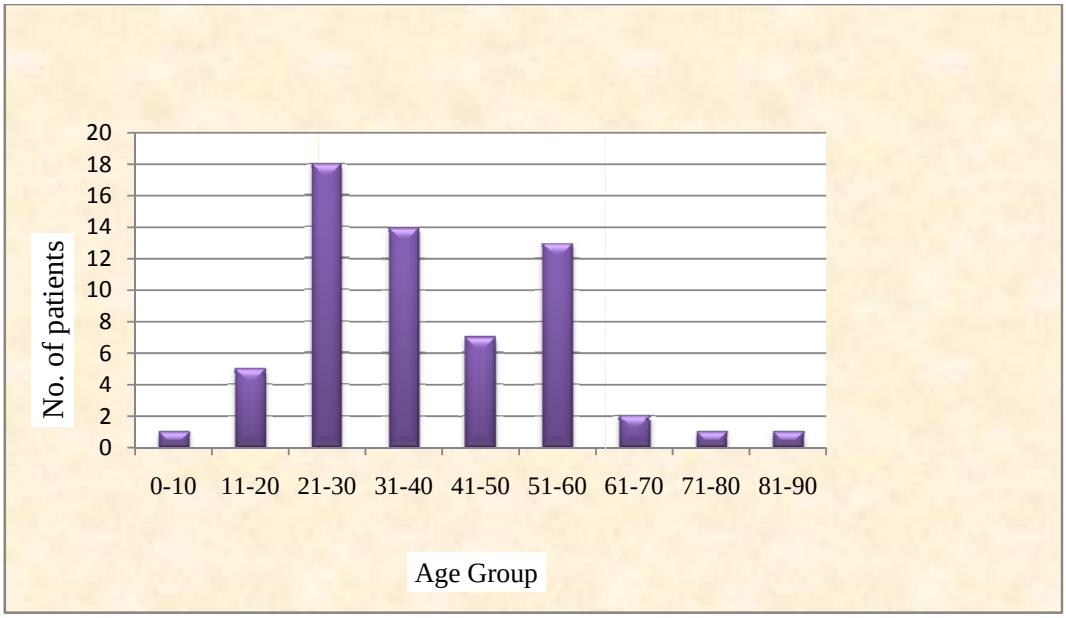
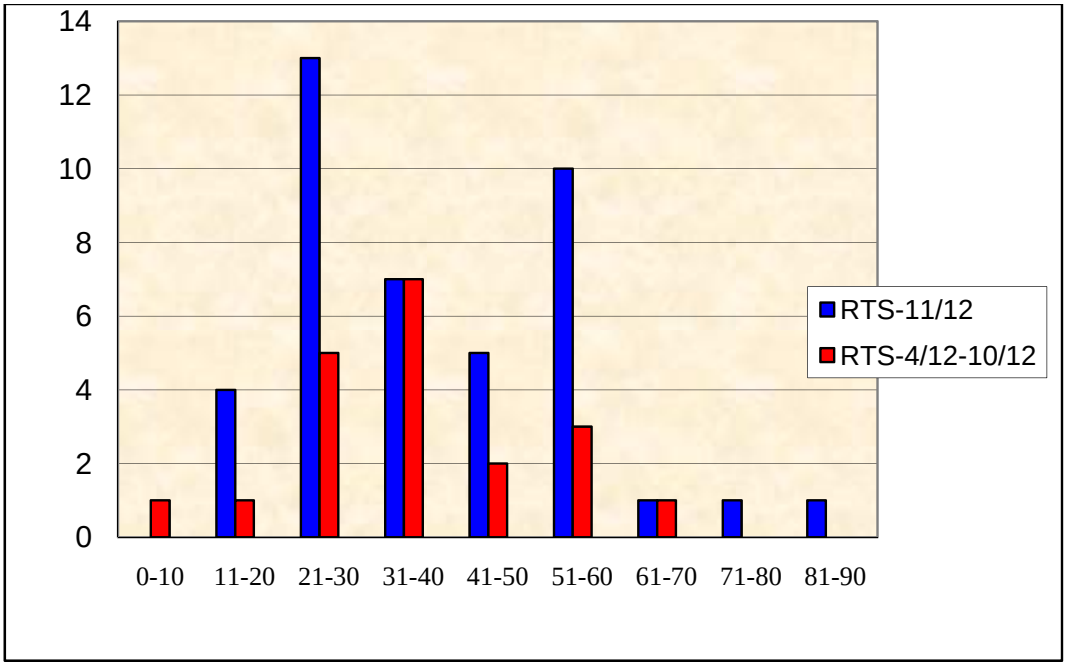


Figure 5 shows the observation of distribution of age of the patients to the severity of injury as indicated by the RTS. 31% patients who had a RTS score of 11/12 [Urgent] were in the 3rd decade, followed closely by patients in the 6th decade [24%]. 60% of patients who had a RTS score between 10/12 and 4/12 [categorized as 'Immediate'] were in the 3rd and 4th decades.

Figure 5: Age distribution of the study population according to the severity of injury



23% of the study population had abnormal results of Prothrombin Time [Table 7]. Prothrombin Time was prolonged in 26% patients who had a RTS score of 11/12 [Urgent] and in 15% patients who had a RTS score between 10/12 and 4/12.

Table 7: Occurrence of abnormal results of PT

RTS score	No. of patients with normal PT [11-15 sec]	No. of patients with prolonged PT [>15 sec]	Total No. of patients
11/12	31	11	42
4/12 to10/12	17	3	20
Total	48	14	62

Only 4.8% of the study population had abnormally increased results of Activated Partial Thromboplastin Time [Table 8]. APTT was prolonged in 2.3% patients who had a RTS score of 11/12 [Urgent] and in 10% patients who had a RTS score between 10/12 and 4/12.

Table 8: Occurrence of abnormal results of APTT

RTS score	No. of patients with normal APPT [27-35 sec]	No. of patients with abnormal APTT [>35 sec]	Total No. of patients
11/12	41	1	42
4/12 to10/12	18	2	20
Total	59	3	62

76% of the study population had abnormal results of D-dimer [Table 9]. D-dimer was prolonged in 76% patients who had a RTS score of 11/12 and in 75% patients who had a RTS score between 10/12 and 4/12.

Table 9: Occurrence of abnormal results of D-dimer

RTS score	No. of patients with Normal D-dimer [<0.5µg FEU/ml]	No. of patients with Abnormal D-dimer [>0.5µg FEU/ml]	Total No. of patients
11/12	10	32	42
4/12 to10/12	5	15	20
Total	15	47	62

11.3% of the study population had thrombocytopenia on admission [Table 10]. Thrombocytopenia was observed in 10% patients who had a RTS score of 11/12 and in 15% patients who had a RTS score between 10/12 and 4/12.

Table 10: Occurrence of low platelet counts

RTS score	No. of patients with normal platelet count [1.5-4.2 lakh /cu.mm]	No. of patients with low platelet count [<1.5 lakh /cu.mm]	Total No. of patients
11/12	38	4	42
4/12 to10/12	17	3	20
Total	55	7	62

Only 3% of the study population had abnormally increased results of both Activated Partial Thromboplastin Time & Prothrombin time [Table 11].

Table 11: Occurrence of abnormal results of APTT and PT

RTS score	No. of patients with either normal APTT/PT or any 1 was abnormal	No. of patients with both APTT & PT abnormal	Total No. of patients
11/12	42	0	42
4/12 to10/12	18	2	20
Total	60	2	62

31% of the study population had anemia [Table 12]. Anemia was observed in 33% patients who had a RTS score of 11/12 and in 25% patients who had a RTS score between 10/12 and 4/12.

Table 12: Occurrence of low hemoglobin values

RTS score	No. of patients with normal Hb [Normal = ≥12g%]	No. of patients with low Hb [<12g%]	Total No. of patients
11/12	28	14	42
4/12 to10/12	15	5	20
Total	43	19	62

21% of patients with normal hemoglobin had abnormal results of either APTT or PT, while 32% of patients with low hemoglobin had abnormal results of either APTT or PT [Table 13].

Table 13: Occurrence of abnormal results of APTT/ PT in patients with normal & low hemoglobin

	No. of patients with….				
RTS score	Hb normal & PT/APTT normal	Hb normal & PT/APTT prolonged	Hb low & PT/APTT normal	Hb low & PT/APTT prolonged	Total No of patients
11/12	20	8	10	4	42
4/12 to10/12	14	1	3	2	20
Total	34	9	13	6	62

81% of the severely injured patients had abnormal results of any 1 of the COT screen parameters i.e., PT, APTT, D-dimer & Platelet count as shown in Table 14. Abnormal results of any 1 or more of these parameters was observed in 83% patients who had a RTS score of 11/12 and in 75% patients who had a RTS score between 10/12 and 4/12.

Table 14: Occurrence of abnormal results of APTT/ PT / D-dimer / Platelet counts

	PT, APTT, D-dimer and Platelets		
RTS score	Number of patients with normal values	Number of patients with abnormal values of any 1 or more	Total No. of patients
11/12	7	35	42
4/12 to10/12	5	15	20
Total	12	50	62

Analysis of the abnormal results of the screening tests for COT and the number of sites of injury [Table 15] showed that of the 22 patients who had injury of only 1 site, 91% had an abnormal result of any 1 of the tests while of the 18 patients who had injury of 2 sites, 72% had an abnormal result of any 1 of the tests. 22 patients sustained injuries of more than 2 organs and 16 of them (73%) had an abnormal result of any 1 of the tests.

Table 15: Occurrence of abnormal results of APTT/ PT / D-dimer / Platelet counts according to the number of sites of injury

Type of injury	No. of patients with normal results of PT, APTT, D-dimer and Platelets	No. of patients with abnormal results of any 1 or more of the following: PT, APTT, D-dimer and Platelets	Total No. of patients
Single organ injury	2	20	22
Two organ injury	5	13	18
More than two organ injury	6	16	22
Total	13	49	62

22 patients sustained head injury. Of these 5 had isolated head injury only and, all 5 of them [100%] showed an abnormal result of any 1 or more of the screening tests for COT. 17 patients had head injury as well as injury of 1 or more of the other sites. Of these 12 patients [71%] had an abnormal result of any 1 or more of the screening tests for COT as shown in Table 16.

Table 16: Occurrence of abnormal results of APTT/ PT / D-dimer / Platelet counts in patients with head injury

Type of injury	No. of patients with normal results of PT, APTT, D-dimer and Platelets	No. of patients with abnormal results of any 1 or more of the following: PT, APTT, D-dimer and Platelets	Total No. of patients
Isolated head injury	0	5	5
Head injury with any other organ injury	5	12	17

DISCUSSION

PSGIMSR Hospital is a tertiary care teaching hospital located at Peelamedu, Coimbatore. The Peelamedu region has witnessed tremendous growth in terms of population and infrastructure. It is a very busy commercial area with roads that are heavily congested. The Avinashi road is the main arterial road of this place and is the main pathway for the rest of the city to exit to neighboring cities. It houses as many as 15 colleges and 8 schools. Road traffic accidents are frequent and many of these patients are brought to the EMD of PSGIMSR Hospital as this hospital offers specialized care 24x7. The EMD receives non-traumatic surgical emergencies and medical emergencies as well. The EMD also serves as an outpatient center after the regular working hours of the hospital and on Sundays.

Of the 8019 patients that reported to the EMD during the study period (5 months & 10 days) 6002 were treated as out-patients or discharged after an observation. Thus the number of patients who were admitted for treatment was 2017 (25%). **Of these admissions, 300 were exclusively trauma patients**. In comparison 1577 patients were admitted in the Department of Emergency Medicine at the JPN Apex trauma center of the All India

Institute of Medical Sciences during the study period.[23] This is five times our admission rate of trauma patients. The JPN Apex trauma center is one of the most advanced trauma care centers and has a strong team of consultants and paramedics trained in trauma care. They cater to Delhi and the entire National Capital Region.

There are many **tools to assess the severity of injury. The Injury Severity Score (ISS)** which was first introduced in 1974 is an anatomical scoring system that provides an overall score for patients with multiple injuries. Each injury is assigned an Abbreviated Injury Scale (AIS) scale and is allocated to one of six body regions (head, face, chest, abdomen, extremities including pelvis and external). Only the highest AIS score in each body region is used. The three most severely injured body regions have their score squared and added together to produce the ISS score.

Its weakness are that any error in AIS scoring increases the ISS error, many different injury patterns can yield the same ISS score and injuries to different body regions are not weighted. Also as a full description of patient is not known prior to full investigation and operation, the ISS (along with other anatomical scoring system) is not useful as a standalone

triage tool.[23] Most of the studies on COT in literature were done in centers where the ISS was used to assess the severity of injury.

Several other anatomical trauma scoring systems exist. These are the New Injury Severity Score (NISS), American Association for the Surgery of Trauma (AAST) Organ Injury Scale (OIS), ICD based Injury Severity Score (ICISS), Anatomic Profile & Penetrating Abdominal Trauma Index (PATI).

The physiologic scoring systems that were used are the Glasgow Coma Score (GCS) and the Trauma Score. The Revised Trauma Score (RTS) was introduced to address the deficiencies of the TS by removing the ambiguous respiratory and perfusion components. **RTS is currently the most widely used Injury Scoring System worldwide** as it is simple to calculate and is proven to be effective in making triage decisions and in predicting hospital outcomes. Further it has a high inter-rater reliability[23].

The **Trauma Score-Injury Severity Score** (TRISS) introduced in 1983 is tool that **combines** anatomic and physiologic parameters to arrive at a calculated probability of survival. The TRISS incorporates the ISS, RTS, patient age, and injury mechanism into an equation that uses established

coefficients determined using large trauma databases. TRISS is valuable in outcomes analysis and research but has no value in the patient care setting[24].

The protocol for trauma care followed in the EMD department of PSGIMSR Hospital involves a primary triage by paramedical personnel followed by an advanced secondary triage system called the Revised Trauma Score (RTS). The Revised Trauma Score was based on the systolic blood pressure, respiratory rate and the Glasgow Coma scale. The Orthopedic surgeon and his team perform the secondary survey where the details of injuries are recorded.

Of the trauma patients who were brought directly to the EMD of PSGIMSRH from the site of trauma, 43(4%) were declared dead on arrival. Approximately 50% of trauma related deaths occur immediately and are usually secondary to severe neurologic injuries or exsanguinations from major blood vessel injuries[24]. These deaths can only be avoided by injury prevention. The second peak of approximately 30% of all deaths occurs during the initial hours post injury and preventing these deaths is the objective of modern trauma care.

28% of the trauma patients received directly at the EMD of PSGIMSR Hospital received severe injuries and had RTS between 4/12 & 11/12. The **study population** which was derived from this group had a **mean RTS of 10.44.** Most of the studies reported in the literature had used the anatomic scoring tool - Injury Severity Score to assess injuries. Our results could not be directly compared with them as the RTS is a physiological assessment of injuries.

87% of our study population (severely injured with Revised Trauma Score ranging from 4/12 to 11/12) **was males with an age range of 7-81 years.** A large cohort of patients with similar injuries that was analyzed by MacLeod Jana, Mauricio Lynn and McKenney Mark et al showed an age range of 1-108 years and 76% of them were males[6]. The increased age range could be due to the increased life expectancy in the developed world. The mean age in their study was 38 years and in our study it was very similar (39 years).

In India trauma due to road traffic accidents is most common in youngsters (2^{nd} and 3^{rd} decades). Most of them ply on two wheelers and violate grossly the traffic rules and regulations[25]. The best way to prevent such injuries is to educate the school students of secondary level about traffic

rules along with the first aid methods. The public also must be educated on the golden-hour period because the quality of care provided during this period has a direct bearing on the final outcome.

About 52% of the patients in our study population were aged between 21 and 40. This is the age group that commutes most by two wheelers. We also observed that there was a high occurrence of trauma related severe injuries in people of 6th decade (24%). This has not been observed in other studies.

The Activated Partial Thromboplastin Time [APTT] is a simple test of the intrinsic pathway of coagulation. **The APTT is used to detect** factor deficiency, screen for lupus anticoagulant and to monitor heparin anticoagulation. It is more sensitive to deficiencies of factor VIII and IX than to deficiencies of factor XI and XII or factors involved in the Common pathway. With most techniques, the test usually yields abnormal results if the plasma level of any of the essential factors is < 15 to 30% of the normal value. The APTT thus detects even mild coagulation disorders[26].

The Prothrombin Time [PT] tests the extrinsic coagulation pathway and if the common pathway is normal (as evidenced by a normal Thrombin Time), it is specific for deficiency of factor VII. PT is prolonged if the requisite factors are < 10% of normal[26]. It is the test most widely used for controlling oral anticoagulant therapy.

Fibrin degradation products are protein fragments of varying sizes that result from the proteolytic action of plasmin on fibrin or fibrinogen. Plasma levels of these fragments are commonly increased in association with Disseminated Intravascular Coagulation (DIC) and fibrinogenolysis, disorders in which their presence is of considerable diagnostic importance. The D-dimer assays are based on the detection of antibodies specific for the cross-linked fibrin fragments with no cross-activity with fibrinogen. There are currently three main methods for D-dimer detection. An enzyme-linked immunosorbent assay (ELISA) is highly sensitive and provides quantitative results. The main disadvantage with this technique is that it is very time consuming and hence cannot be used in trauma care centers or for rapid screening for venous thromboembolic disease. The latex agglutination assays are more rapid but have a lower sensitivity of 80%. Quantitative automated latex assays which use special equipment to

measure the decrease in light transmittance at 405nm, have the advantage of being sensitive and also rapid. The COBAS Integra- 400 equipment used to assay D-dimer in our institute is an even more recent and improvised version employing immunoturbiditimetric technique using transmittance at 659nm[27]. It has a sensitivity of 98% and the results are obtained in 15 minutes. Thus D-dimer assay was included in our screening tool for detecting abnormality of coagulation.

There has been a **wide variation in literature on the definition of coagulopathy.** Most commonly used parameters were PT and APTT. The one-stage PT of Quick was the most commonly used test in most of the initial studies. As there was lack of standardization of the thromboplastin preparations, the PT results had led to great discrepancies in the reported results. The use of ISI, the International Sensitivity Index, to assess the sensitivity of any given thromboplastin, and the use of INR, the International Normalized Ratio, to report the results, had minimized these difficulties and greatly improved uniformity of interpretation throughout the world. Thus many recent studies expressed PT results as INR values as shown in table 17.

Table 17: Overview of definitions of Coagulopathy adopted by studies on COT, including the present study

Name of PI of study	Year of study	Definition of Coagulopathy
Selladurai BM	1997	Increase in PT / APTT / TT / FDP* or decrease in fibrinogen / platelet count compared to normal controls in local population. Single values for each of the tests were not specified.
Karim Brohi	2003	PT >18 sec / APTT > 60 sec
Jana MacLeod	2003	PT >14 sec / APTT > 35 sec
Maegele M	2007	Quick test <70% of the lab control
Karim Brohi	2007	PT >18 sec / APTT > 60 sec
Rugeri L	2007	INR >1.6 / APTT > 60 sec
David Hoyt	2008	PT>14 sec / APTT >35 sec / INR >1.6 / Platelet count <1 lakh/cu.mm
John Hess	2009	PT ratio ≥1.3 / APTT >35 / fibrinogen < 2g/l / platelet count <1.5 lakh/cu.mm
Current study	2011	PT>15 sec / APTT>35 sec / D-dimer >0.5µgFEU/ml / platelet count < 1.5 lakh/cu.mm

*FDP = Fibrin Degradation Product

The Prothrombin time was estimated using the fully automated coagulation analyzer- Stago STA Compact. We used a new lot of tissue thromboplastin exclusive for the study population to avoid variations in values caused by different lots with different International Sensitivity Index (ISI). Hence this obviated the need for estimating the International Normalized Ratio (INR). Further, we established the normal PT range by standard protocols using blood samples from 20 healthy controls, 10 of which were men and 10 were women. The PT range was established as 11-15 seconds with a mean PT value of 13 seconds. Hence we used 15 seconds as the cut off for normal limits of PT. The normal range for APTT established in the Clinical Pathology laboratory is 27-35 seconds. Population studies on the normal ranges for platelet counts have not been performed in our center. Hence we used the normal range for platelets published in a standard text book of Clinical Hematology- 1.5-4.2 x $10^3/\mu l$[28]. The same range is reflected in the laboratory results as well. Hence results with platelet count <1.5 X $10^3/\mu l$ was considered abnormal.

23% of the severely injured patients had abnormal results of PT while 4.8% had abnormal results of APTT. The mean values of PT and APTT in the study showed abnormal result for PT (16.6 sec) while APTT was

normal (26.8 sec). **Many studies have shown similar trends** i.e. occurrence of abnormal PT was more than that of abnormal APTT. For instance, in the Miami study 28% of the severely injured patients had an abnormal PT compared with 8% of patients with an abnormal APTT[6]. The Miami study also observed the mortality associated with these abnormal results. They found that an abnormal APTT had an adjusted odds ratio of death of 4.26, compared with 1.54 for an abnormal PT. One of the largest reviews of trauma registry parameters from 1995 to 2000 showed that the top four predictors of mortality were APTT (OR,3.37;95%CI:2.51-4.52), positive head computed tomography results (OR,2.2;95%CI:1.95-3.04), initial hemoglobin (OR,1.69;95%CI:1.23-2.31), base deficit (OR,1.62;95%CI:1.29-2.04) and trauma resuscitation bay systolic blood pressure (OR,1.45;95%CI: 1.11-1.88)[8].

Only 2 patients of the study population had abnormal levels of both PT and APTT. Both of these had a RTS ranging from 4/12 to 10/12. They sustained multiple organ injuries and one of them had a head injury as well. In the hypoperfusion study of Karim Brohi et al, they observed that patients with either an abnormal PT or APTT received a mean of 10 units of blood compared with those with normal values for both tests[29].

However, if both PT and APTT were abnormal, the mean number of units of blood used to treat them was 13.

Spahn and Rossaint suggest that the incidence of abnormal results of coagulation, especially those of PT and APTT may be much higher than what is observed. This is because the coagulation process is temperature dependent and functions optimally at 37^0C. Patients with severe injuries often are hypothermic. Blood drawn from these patients is warmed to 37^0C prior to testing which causes normalcy of coagulation function resulting in spurious normal values. If these tests are carried out at low temperatures, as seen in vivo in hypothermic patients both are significantly prolonged[9]. In addition both in vivo and in vitro studies have shown that hypothermia significantly impairs platelet function and the formation of platelet plug and activates fibrinolysis.

Assays of D-dimers to identify defects in fibrinolytic pathway of coagulation have been historically hampered by the methods used to assay it. Gandos et al have observed that D-dimer levels were elevated in all patients presenting with a Disseminated Intravascular Coagulation like picture where the diagnosis was made on clinical grounds and confirmed hours later by laboratory results[30]. They had estimated D-dimer levels by

ELISA method which was time consuming and therefore not practicable in acute trauma situations. We have assayed D-dimers by immunoturbidimetry and observed that 76% of the study population (the severely injured patients who were categorized as urgent / immediate) had raised D-dimer levels. **The mean D-dimer value in the study group was 2.49µgFEU/ml (Normal = <0.5 µgFEU/ml).** John Hess et al in their study assayed fibrinogen levels and found the prevalence of abnormal results increased with severity of injury[18]. **Hyperfibrinolysis is common after trauma and is a direct consequence of both tissue injury and shock.** Endothelial injury results in increased fibrinolysis because of the direct release of tissue plasminogen activator (tPA). Fibrinolysis is exacerbated because of the combined effects of endothelial tPA released due to ischemia and inhibition of plasminogen activator inhibitor-1 (PAI-1) in shock[15].

7 of the 62 patients had platelet count <1.5lakh/cu.mm and the lowest platelet count observed was 33000/cu.mm. This patient had abnormal results of all the other three screening tests (PT, APTT and D-dimer) and his hemoglobin on admission was 5mg/dl. He had sustained head injury,

injury to both lower limbs and had neurovascular deficits. He was treated as acute DIC and died 6 hours after admission. Only 2 patients had abnormal results of both PT and APTT one of whom had severe thrombocytopenia and was discussed in the previous paragraph. The second patient also had thrombocytopenia (73,000/cu.mm) and had sustained head injury as well as injuries to abdomen and pelvis. This patient also had abnormal D-dimer levels and had hemoglobin of 6gm/dl on admission. Incidentally, this patient also died within 24 hours of admission.

19 patients of the study group presented with anemia although the mean hemoglobin of the group was 12.6gm/dl. More patients with low hemoglobin had abnormal results of either APTT or PT than those with normal hemoglobin. Jana MacLeod et al had also observed that initial low hemoglobin was one of the top 4 predictors of mortality and was independent in the presence of all other factors. This was a treatable risk factor and timely availability of blood was crucial to survival[8].

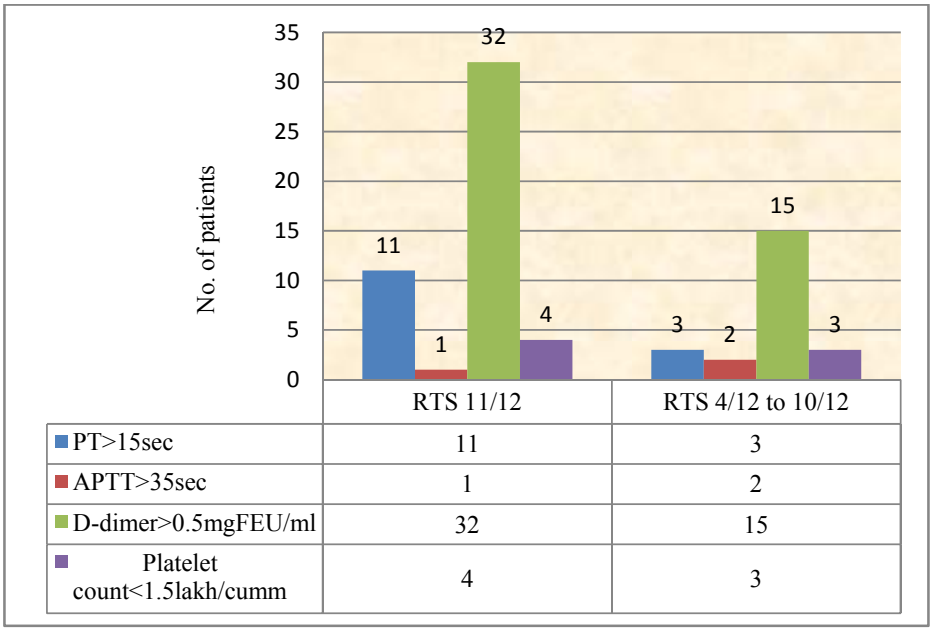
The most attention-grabbing results of our study were noted when we observed results of all the four screening tests (PT, APTT, D-dimer

and platelet count) as a combination, in the study population. 50 patients (72%) had an abnormal result of any one of the tests as shown in figure 6. We therefore feel that it is essential to perform all the screening tests for COT as it has significant pick up rate of identifying COT. One of the limitations of our study is that we have not observed the association of these abnormal results of coagulation with mortality.

Maegele Marc et al observed that 70% of the severely injured trauma patients had abnormal results of screening tests for coagulation if they were treated with large volumes of intravenous fluids[12]. He had not observed the results of screening tests for coagulation on admission, prior to initiation of treatment.

Karim brohi et al suggest that in addition to the routine screening tests in coagulation, plasma soluble thrombomodulin and Protein C assays may also be useful in the initial screen as they have also shown to be predictors of mortality.

Figure 6: Distribution of abnormal results of coagulation observed in the study population



	RTS 11/12	RTS 4/12 to 10/12
PT>15sec	11	3
APTT>35sec	1	2
D-dimer>0.5mgFEU/ml	32	15
Platelet count<1.5lakh/cumm	4	3

The study conducted by Kanchana Rangarajan et al at All India Institute of Medical Sciences, New Delhi, have shown that DIC scores (as evidenced by low platelet counts, elevated fibrin related marker, prolonged PT and decreased fibrinogen levels), were minimally deranged (18%) at the time of admission and increased slightly with surgical intervention (26%). However their PT cut off was 20.5 seconds and the APTT cutoff was 48 seconds. This is probably the reason why their detection rate of coagulopathy upon admission was lower than ours. They also observed that COT results did not correlate with ISS scores.

We attempted to identify if there was any correlation between the abnormal results of coagulation and the number of sites of injury. We did not observe a consistency in the results. For instance, 91% of patients with injury to a single site had abnormal results of coagulation while 72% of patients with injury to two sites had abnormal results. 73% of patients with injuries to more than two sites had abnormal results of coagulation. It is well known that there is a wide variation in the amount of tissue damage in traumatic injuries. For a given site, crush or explosion injuries may carry an enormous tissue injury load than lethal penetrating trauma. Patients with severe tissue injury but without physiologic derangements rarely presented with a coagulopathy and had a relatively low mortality rate. Long bone fractures and fat embolism syndrome are rare causes of DIC-like picture, but they are rare in early stages after injury. Multiple long bone fractures had a higher incidence of coagulopathy through simple tissue injury, shock and inflammation, rather than through a bone marrow-specific pathogenesis[15].

We observed a 100% occurrence of abnormal results of coagulation in patients with isolated head injury. However only 71% of patients who

had head injury and injury to any other site had abnormal results. We have not followed all the cases of head injury for an adverse event outcome, such as mortality. However we followed the 2 cases which had abnormal results of all the tests of coagulation and both of them had died.

Selladurai et al observed that 71% of patients with acute head injury had at least one abnormal result of coagulation. Their study included analysis of all the 4 parameters that we have analyzed in our study. They had in addition performed fibrinogen assay. The results of the coagulation screen tests were extrapolated to a DIC score. They found that the Glasgow Coma Scale correlated inversely with the DIC[31].

Pathak A et al provided quantitative data on tissue thromboplastin activity of normal brain and highlighted the role of tissue thromboplastin in coagulopathy following head injury through its increased activity after head injury, especially so in the severe head injury group[11].

Peep Talwing et al also observed a high incidence of COT (34%) in patients with severe head injury, especially in penetrating injuries. This is lower than what we have observed in our study. Peep Talwing also

identified that independent risk factors for coagulopathy in isolated head injuries included a GCS $\leq$ 8, ISS $\geq$16, hypotension upon admission, cerebral edema, subarachnoid hemorrhage and midline shift. They noted that the development of COT in traumatic brain injury was associated with longer ICU length of stay and an almost ten-fold increased risk of death[17].

John Olson et al also have proved that the screening tests for coagulation are reliable predictors of outcome in patients with head injury. The highest degree of accuracy was noted with high DIC scores. The degree of increase of initial D-dimer levels and prolongation of thrombin clotting time and APTT also correlated positively with the outcome[32].

SUMMARY & CONCLUSIONS:

The objective of the study was to observe the occurrence of 'Coagulopathy of Trauma' in severely injured trauma patients, by examining the results of the basic screening tests for coagulation, such as Prothrombin Time [PT], Activated Partial Thromboplastin Time [APTT], D-dimer and Platelet count.

The study population was 62 patients with severe injuries [i.e. Revised Trauma Score between 4/12 & 11/12], admitted directly to the Emergency Medicine Department of PSGIMSR Hospital. We found that most of these patients were aged between 21 & 40 years and that most of them were males.

23% of the patients had abnormal results of PT, while 4.8% had abnormal results of APPT. However, 76% had abnormal results of D-dimers, thus highlighting that a fibrinolytic activity existed in most patients with severe injuries. 11.3% had thrombocytopenia on admission.

81% of the study population had abnormal results of any 1 of the screening tests for coagulation. Hence we recommend that it is essential

to perform these screening tests in all trauma patients with severe injuries to identify the coagulopathy of trauma, so that, the patients are provided with appropriate evidence-based therapy.

All the 5 patients who had isolated head injuries had abnormal results of any 1 of the screening tests for coagulation. Of these, 2 patients had abnormal results of all the 4 parameters and died within 24 hours of admission. This substantiates the current practice in neurosurgery, to perform the screening tests for coagulation for all patients with head injury, however trivial it might be on physical examination.

Further studies are essential to correlate abnormal results of screening tests for coagulation in severely injured trauma patients, with outcomes such as duration of hospital stay, morbidity and mortality.

BIBLIOGRAPHY

1. Murray.CJ , Lopez AD. Mortality by causes for eight regions of the world: Global burden of disease study. Lancet 1997; 349 : 1269-76.
2. Gururaj G. Injuries in India : A national perspective. National Commission on Macroeconomics and Health Background Papers- Burden of Disease in India- Ministry of Health and Family Welfare, Government of India, New Delhi; September 2005: 325-350.
3. Mortality Country Fact Sheet 2006, India ,World Health Organization; http://www.who.int/whosis/mort/profiles/mort_searo_ind_india.pdf
4. Angela Sauaia, Frederick A Moore, Ernest E Moore et al. Epidemiology of Trauma Deaths: A Reassesment. The Journal of Trauma- Injury Infection & Critical Care: February 1995; vol 38; Issue 2: 185-193
5. Ned Cosgriff, Ernest E Moore, Angela Sauaia et al. Predicting Life-threatening Coagulopathy in the Massively Transfused Trauma Patient: Hypothermia and Acidosis Revisited. The Journal of Trauma- Injury Infection & Critical Care: May 1997; vol 42; Issue 5: 857-862.

6. Macleod Jana B.A, Lynn Mauricio, McKenney Mark G et al. Early Coagulopathy Predicts Mortality in Trauma. The Journal of Trauma-Injury Infection & Critical Care: April 2003; vol 55; 39-44.
7. Karim Brohi, Jasmine Singh, Mischa Heron et al. Acute Traumatic Coagulopathy. The Journal of Trauma- Injury Infection & Critical Care: June 2003; vol 54; Issue 6: 1127-1130.
8. Macleod Jana B.A, Lynn M, McKenney MG et al. Predictors of mortality in trauma patients. American Journal of Surgery: September 2004; vol 70; Issue 9: 805-810.
9. Spahn.D.R, Rossaint.R. Coagulopathy and blood component transfusion in trauma. British Journal of Anaesthesia: June 2005; vol 95; Issue 2: 130-139.
10. Peng RY, Bongard FS. Hypothermia in Trauma patients. Journal of American College of Suergons: June 1999; vol 188; Issue 6: 685-696.
11. Pathak.A, Dutta.S, Marwaha.N et al. Change in tissue thromboplastin content of brain following trauma. Neurology India: June 2005; vol 53; Issue 2: 178-182.
12. Maegele Marc, Lefering Rolf, Yucel Nedim et al. Early coagulopathy in multiple injury: An analysis from the German

Trauma Registry on 8724 patients. International journal of the Care of the Injured: October 2006; vol 38; Issue 3: 298-304.

13. Karim Brohi, Mitchell J. Cohen and Ross A. Davenport. Acute coagulopathy of trauma: mechanism, identification and effect: Current Opinion in Critical Care; 2007; vol 13: 680-685.
14. Robert C Jacoby, John T Owings, James Holmes et al. Platelet Activation and Function after Trauma: The Journal of Trauma-Injury Infection & Critical Care: October 2001; vol 51; Issue 4: 639-647.
15. Hess John R, Karim Brohi, Dutton Richard P et al. The Coagulopathy of Trauma: A Review of Mechanisms: The Journal of Trauma- Injury Infection & Critical Care: July 2008; vol 65: 748-754.
16. David B Hoyt, Dutton Richard P, Carl J Hauser et al. Management of Coagulopathy in the Patients With Multiple Injuries: Results From an International Survey of Clinical Practice: The Journal of Trauma- Injury Infection & Critical Care: October 2008; vol 65; Issue 4: 755-765.
17. Peep Talving, Rodd Benfield, Pantelis Hadjizacharia et al. Coagulopathy in Severe Traumatic Brain Injury: A Prospective

Study: The Journal of Trauma- Injury Infection & Critical Care: January 2009; vol 66; Issue 1: 55-62.

18. Hess John R, Lindell Alission L, Stansbury Lynn G et al. The prevalence of abnormal results of conventional coagulation tests on admission to a trauma center: Transfusion: January 2009; vol 49: 34-39.
19. Ganter MT, Pittet JF. New insight into acute coagulopathy in trauma patients: Best Practical Research in Clinical Anaesthesiology: March 2010; vol 24; Issue 1: 15-25.
20. Kanchana Rangarajan, Arulselvi Subramanian, Jatin S Gandhi et al. Coagulation Studies in patients with orthopedic trauma: Journal of Emergencies, Trauma, and Shock: January 2010; vol 3; Issue 1: 4-8.
21. Pierre Taboulet, Veronique Moreira, Laurent Haas et al. Triage with the French Emergency Nurses Classification in Hospital scale: reliability and validity: European Journal of Emergency Medicine: 2009; vol 16;61-67.
22. Jai Prakash Narayan Apex Trauma Center- All India Institute of Medical Sciences; http://www.jpnatc.com/department.emergency.asp

23. Trauma Scoring: Injury Severity Score; http://www.trauma.org/archive/scores/iss.html
24. The Trauma Manual: Trauma and Acute Care Surgery. Andrew B Pietzman, Michael Rhodes, William Schwab et al. Lippincott Williams and Wilkins, 3rd edition, 2008: 1-15.
25. Textbook of Trauma. Pramod Kumar. CBS Publishers and Distributors. 1st edition,2011: 1-5
26. Wintrobe's Clinical Hematology. Edited by John Geer, John Foester, George Rodgers et al. Lippincott Williams and Wilkins. 12th edition,2009 : 1279-1280.
27. The Science of Laboratory Diagnosis- Edited by John Croker and David Burnett. John Wiley & Sons, Ltd. 2nd edition, 2005:335-339.
28. Dacie and Lewis Practical Hematology. Lewis, Bain and Bates. Churchill Livingstone. 10th edition,2006: 11-25.
29. Brohi K, Cohen MJ, Genter MT et al. Acute Traumatic Coagulopathy: initiated by hypoperfusion: modulated through the Protein C pathway? Annals of Surgey 2007; 245:812-818.
30. Satoshi Gando, Ichiro Tedo & Munehiro Kubota. Posttrauma coagulation and fibrinolysis. Critical Care Medicine 1992:20:594-600.

31. Selladurai BM, Vickneswaran M, Duraisamy S & Atan M. Coagulopathy in acute head injury – a study of its role as a prognostic marker. British Journal of Neurosurgery 1997; 11(5):398
32. John Olson, Howard Kaufman, Joel Moake et al.The incidence and significance of hemostatic abnormalities in patients with head injuries. Neurosurgery 1989; 24:825-832.

COT STUDY – MASTER CHART

S.No	Name	ID	Age	Sex	Date of admission	Site of Injury	RTS			Total RTS	PT (sec)	APTT (sec)	D-dimer (µg FEU/ml)	Platelet count (x 10^3/cu.mm)	Hg (g/dl)
							Systolic BP	Resp rate	GCS						
1	Karthikeyani	O11005986	23	F	26/01/11	7	4	3	4	11	13.6	36.6	0.5	2.4	13.2
2	Ramalakshmi	O11006025	52	F	26/01/11	5	3	4	4	11	13.6	26.9	0.5	2.8	14
3	Rasammal	O11006076	40	F	26/01/11	7,8	4	3	4	11	14.6	25.3	3.1	2.5	9.2
4	Kuppusamy	O11006102	65	M	26/01/11	6,7	3	4	4	11	14.9	25.6	0.4	2.92	6.6
5	Indirani	O11007562	56	F	29/01/11	7	3	4	4	11	11.7	27.6	6.01	1.54	11.6
6	Karuppusamy	O11007567	45	M	29/01/11	7	4	3	4	11	13	29.4	1.25	2.1	11
7	Kanakasapapati	O11007680	57	M	30/01/11	7	4	3	4	11	13.2	25.8	2.4	2.55	14.8
8	Natrajan	O11007703	58	M	30/01/11	7,9	3	4	4	11	13.3	28.5	1.24	3.2	13.4
9	Ramasamy	O11007701	56	M	30/01/11	7,9	4	3	3	10	14	25.3	>9	1.73	11.4
10	Dhandapani	O04050604	66	M	31/01/11	1, 5, 7	1	2	2	5	22.2	48.2	9	0.73	6
11	Siva	O11008330	19	M	1/2/2011	7	4	3	4	11	13.5	25.3	1.2	3.1	14
12	Raja Mohd.	O11009438	26	M	6/2/2011	7	4	3	4	11	16.6	22.4	2.9	1.91	13.9
13	Ramachandran	O11012142	41	M	16/02/11	9	4	3	4	11	14.2	24.4	6.3	1.99	10.5
14	Ramesh	O11012747	27	M	18/02/11	5,8	4	3	4	11	16	29.1	>9	1.83	10.3
15	Jayeseelan	O11013424	54	M	21/02/11	7	4	4	1	9	13.2	23.7	>7	1.97	16.4
16	Mohd. Sahith	O11013869	26	M	22/02/11	7	3	4	4	11	15.3	25.2	0.9	2.89	13.9

Codes used: GCS = Glasgow Coma Score; RTS = Revised Trauma Score; Codes used in site of injury column: 1= head injury, 2 = facial injury, 3 = dental injury, 4 = chest injury, 5 = abdomen & pelvis, 6 = spine injury, 7 = limb injury, 8 = bony injury & 9 = neurovascular deficit

COT STUDY – MASTER CHART

S.No	Name	ID	Age	Sex	Date of admission	Site of Injury	RTS			Total RTS	PT (sec)	APTT (sec)	D-dimer (mg FEU/ml)	Platelet count(x 10^3/cu.mm)	Hg (g/dl)
							Systolic BP	Resp rate	GCS						
17	Shakthivel	O11014421	35	M	23/2/11	7,8	3	4	4	11	13.6	26.7	1.1	2.05	16.1
18	Hausenthu	O11014425	27	M	24/2/11	7	3	4	4	11	13.7	25.3	4.4	2.2	16.3
19	Nagaraj	O11014698	23	M	24/2/11	7	3	4	4	11	13.4	26.7	0.9	1.9	14
20	Rajasundaram	O11015783	29	M	1/3/2011	5,7	3	4	4	11	12.4	25.4	0.4	2.7	13.1
21	Iqbal	O11016034	35	M	1/3/2011	5,7	3	4	4	11	17.2	31.1	3.2	2.5	14.5
22	Manikandan	O11028610	30	M	2/3/2011	7	3	4	4	11	13	27.6	0.4	3.2	14.2
23	Venkatasamy	O11016746	75	M	4/3/2011	7,8	3	4	4	11	14.2	24.6	>9	1.11	10.1
24	Murugadass	O11016793	40	M	5/3/2011	7	4	3	4	11	16.9	27.7	7.4	2	10.5
25	Vijayakumar	O11017047	40	M	6/3/2011	1,4,5,7,8, 9	4	4	2	10	14.9	24.3	>9	1.67	12.8
26	Saravanan	O11017053	32	M	6/3/2011	2,7	4	4	2	10	11.7	22.8	0.5	2.9	16.5
27	Sivasamy	O01019828	60	M	6/3/2011	7,8	2	3	3	8	14	21.6	3.5	2.23	14.1
28	Raja	O11017081	37	M	7/3/2011	2,7	3	4	4	11	27.9	13.3	4.4	2.44	13.9
29	Marappan	O05004400	81	M	8/3/2011	1	3	4	4	11	25.3	14.2	0.5	1.84	10.4
30	Mukesh	O11017809	20	M	9/3/2011	2,7	3	4	4	11	13.8	26.3	0.3	3.4	13.9
31	Moorthy	O11017865	56	M	9/3/2011	1,2	4	4	3	11	14	24.1	>7	4.3	10.4
32	Krishnaraj	O11018234	40	M	10/3/2011	1,2	4	4	2	10	15	24	2.6	4.36	12.9

Codes used: GCS = Glasgow Coma Score; RTS = Revised Trauma Score; Codes used in site of injury column: 1= head injury, 2 = facial injury, 3 = dental injury, 4 = chest injury, 5 = abdomen & pelvis, 6 = spine injury, 7 = limb injury, 8 = bony injury & 9 = neurovascular deficit

COT STUDY – MASTER CHART

S.No	Name	ID	Age	Sex	Date of admission	Site of Injury	RTS			Total RTS	PT (sec)	APTT (sec)	D-dimer (g FEU/ml)	Platelet count(x 10^3/cu.mm)	Hg (g/dl)
							Systolic BP	Resp rate	GCS						
33	Piyarisha	O11018846	7	F	13/3/11	1,7,8	3	3	3	9	14.9	26.7	0.9	2.76	11.3
34	Rajkumar	O11021171	28	M	22/3/11	1,5,7	4	3	4	11	15	26.9	0.4	2.61	12.4
35	Karthkumar	O11023585	36	M	24/3/11	1,2,7	3	3	3	9	13	26.8	0.3	3.32	12.9
36	Rajamohan	O11022278	31	M	25/3/11	2,3,7,9	3	3	4	10	14.4	28.3	0.4	2.32	14.1
37	Rathinasamy	O11022130	42	M	25/3/11	1,2	3	4	3	10	14.9	26.1	6.6	1.66	12.4
38	Rajapriya	O11022277	24	F	25/3/11	2,3,7	3	4	4	11	15.3	28.8	6.8	1.3	12.1
39	Palanisamy	O11022292	40	M	25/3/11	1,7,9	4	3	4	11	13.9	27.6	5.5	2.26	12.2
40	Karthikeyan	O11022621	23	M	26/3/11	1,7	4	4	3	11	14.2	24.2	0.4	1.54	12
41	Madanmohan	O11022299	60	M	26/3/11	2,8,9	3	4	4	11	15.5	23.7	>8	1.23	12.5
42	Eswaran	O11020920	42	M	27/3/11	2,5,7	3	4	4	11	12.5	29	1.6	2.07	13.1
43	Muthu	O11023190	54	M	29/3/11	7	3	4	4	11	13.3	26.3	>8	2.42	15.2
44	Manoharan	O11024094	30	M	30/3/11	2,4,7,8,9	3	3	3	9	15.9	28	>8	1.89	13
45	Murugesan	O11023821	32	M	31/3/11	1,2,4,7	3	3	3	9	13.2	25	0.3	2.96	14.8
46	Sangari	O11024085	17	F	31/3/11	1	4	3	4	11	15.2	30.3	0.4	2.07	13.1
47	Nandakumar	O11024162	22	M	1/4/2011	2,5,7,8	4	4	3	11	20.8	27.2	>7	1.7	10.3
48	Loganathan	O11025260	35	M	5/4/2011	4,5,7	3	4	4	11	14.2	27.5	>9	1.94	13

Codes used: GCS = Glasgow Coma Score; RTS = Revised Trauma Score; Codes used in site of injury column: 1= head injury, 2 = facial injury, 3 = dental injury, 4 = chest injury, 5 = abdomen & pelvis, 6 = spine injury, 7 = limb injury, 8 = bony injury & 9 = neurovascular deficit

COT STUDY – MASTER CHART

S.No	Name	ID	Age	Sex	Date of admission	Site of Injury	RTS			Total RTS	PT (sec)	APTT (sec)	D-dimer (mg FEU/ml)	Platelet count(x 10^3/cu.mm)	Hg (g/dl)
							Systolic BP	Resp rate	GCS						
49	Kandasamy	O11025509	48	M	6/4/2011	2,7,8	3	4	4	11	13.1	21.2	6.1	1.86	13.2
50	Nemathulla	O11025512	50	M	7/4/2011	1,2,7	4	4	3	11	12.7	29.9	0.7	1.92	12.6
51	Bizumoon	O11026277	27	M	10/4/2011	1,7,9	4	4	1	9	128	42.6	>6	0.33	5
52	Kaliammal	O11026252	55	F	10/4/2011	1	4	3	4	11	12.6	24.8	3.8	2.58	11.8
53	Manikandan	O11026596	13	M	11/4/2011	1	4	3	4	11	14.5	26.3	1.4	1.73	11.4
54	Parthiban	O11009441	21	M	6/5/2011	2,7	4	4	2	10	14	30.5	2.9	2.65	13
55	Dhayanandhan	O11047830	20	M	7/5/2011	1,2,7,8,9	3	3	3	9	13.7	28.6	0.4	2.5	16.4
56	Prema	O11018786	55	F	12/5/2011	1	4	3	4	11	13.2	25	3	2.36	9.6
57	Suresh	O11044547	25	M	23/6/11	1,2,7	3	3	4	10	14.4	26.7	1	2.03	15.3
58	Arulraj	O11044551	41	M	23/6/11	1,4,7	3	3	4	10	14.8	29.9	2.3	2.59	15.5
59	Prasanth	O11044583	24	M	23/6/11	7	3	4	4	11	14.5	28.1	0.6	2.62	14
60	Kalimuthu	O11044641	55	M	23/6/11	7	4	4	3	11	13.4	25	2.1	1.42	12.8
61	Kaliraj	O11044573	29	M	23/6/11	1,2,3,4,5, 6,7,8	3	3	4	10	14.2	24.6	>8	0.83	11.7
62	Vijayamohan	O11046103	38	M	29/6/11	1,2,6,7,8, 9	4	3	2	9	14.7	29.4	6.7	4.41	11.2

Codes used: GCS = Glasgow Coma Score; RTS = Revised Trauma Score; Codes used in site of injury column: 1= head injury, 2 = facial injury, 3 = dental injury, 4 = chest injury, 5 = abdomen & pelvis, 6 = spine injury, 7 = limb injury, 8 = bony injury & 9 = neurovascular deficit